

POLYPEPTIDE VARIANTS WITH ALTERED
EFFECTOR FUNCTION

Leonard Presta

Serial No.: To Be Assigned

Docket No. P1726R1D1

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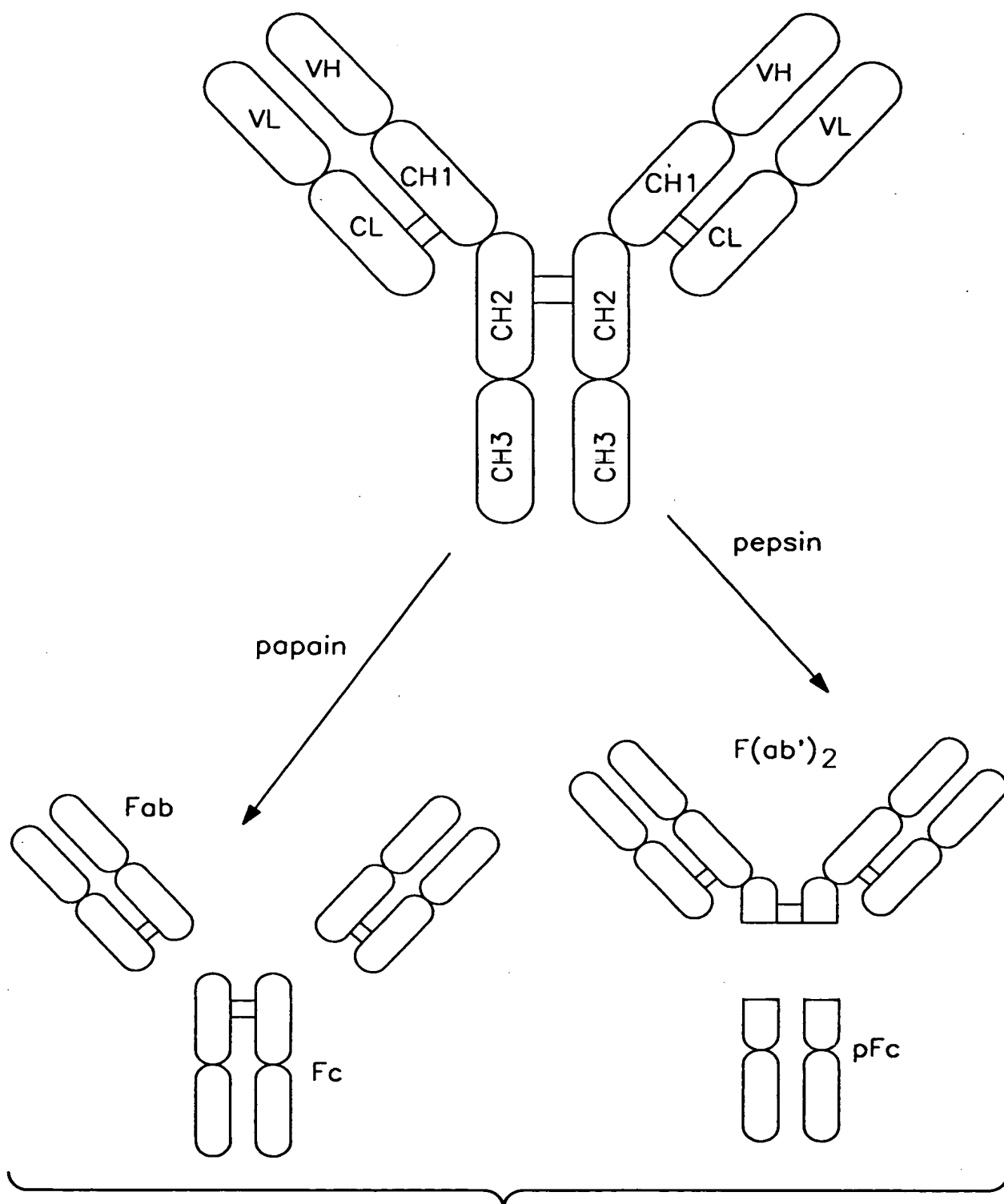


FIG. 1

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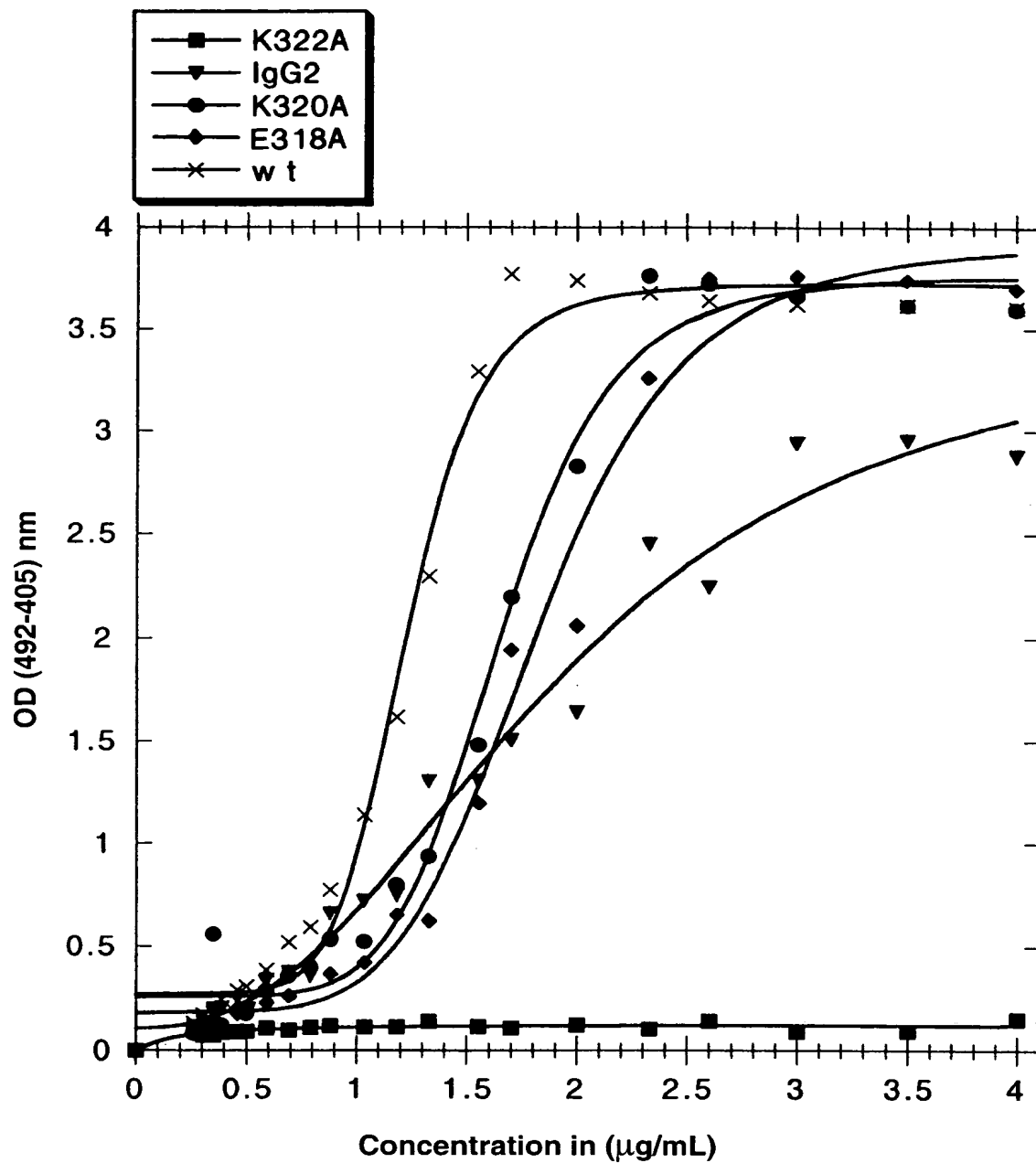


FIG. 2

POLYPEPTIDE VARIANTS WITH ALTERED
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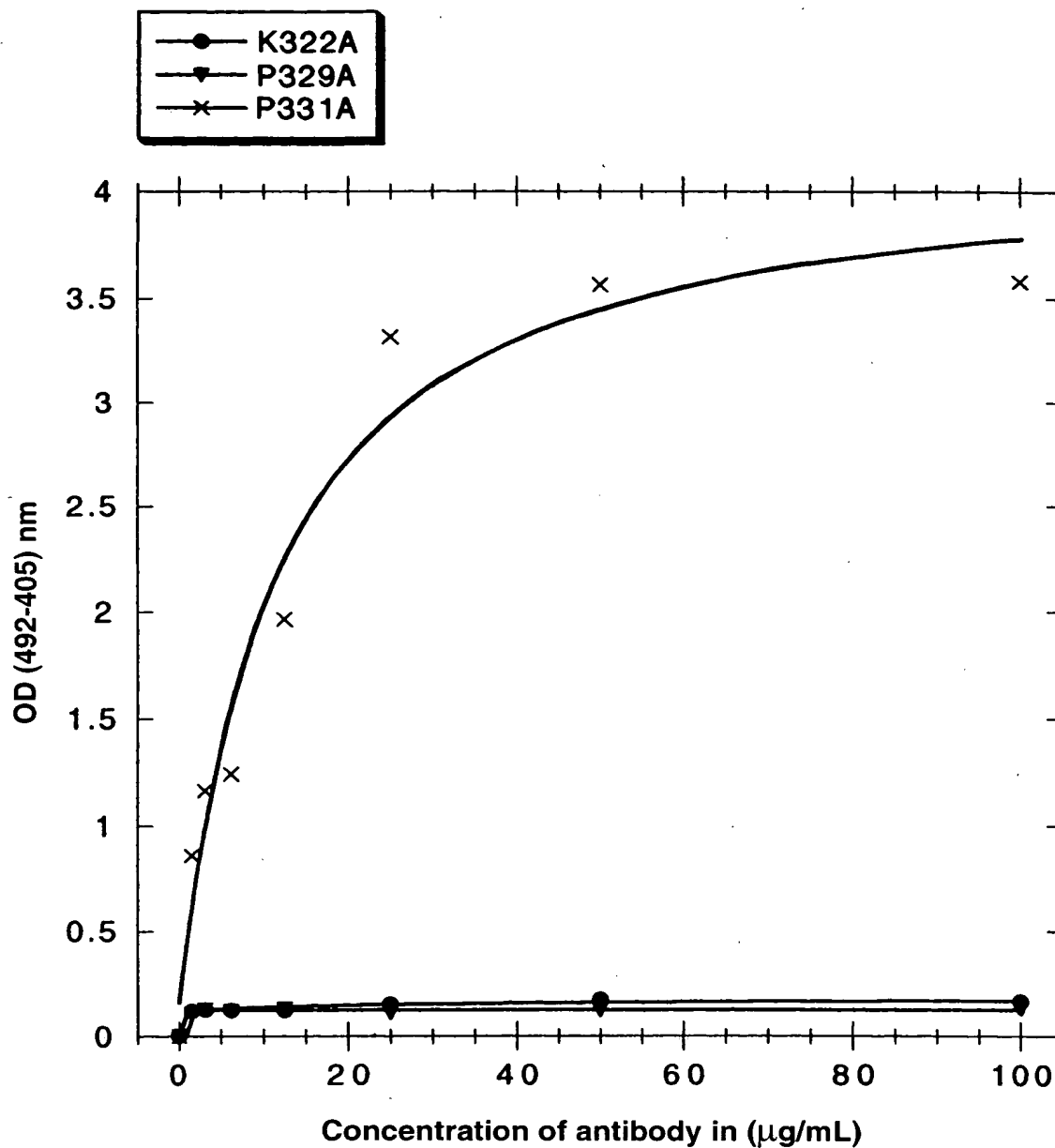


FIG. 3

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(E27) - Light Chain

DIQLTQSPSS LSASVGDRVT ITCRASKPVD GEGDSYMNWY QQKPGKAPKL LIYAASYLES GVPSRFSGSG
SGTDFTLTIS SLQPEDFATY YCQQSHEDPY TFGQGTKVEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL
NNFYBREAKV QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLKADY EKHKVYACEV THQGLSSPVT
KSFNRGEC

FIG._4A

(E27) - Heavy Chain

EVQLVESGGG LVQPGGSLRL SCAVSGYSIT SGYSWNWIRQ APGKGLEWVA SIKYSGETKY NPSVKGRITI
SRDDSKNTFY LQMNSLRAED TAVYYCARGS HYFGHWHFVAV WQGTLVTVS SASTKGPSVF FLAPSSKSTS
GGTAALGCLV KDYFPEPTV SWNSGALTSG VHTFPAVLQS SGLYSLSSV TVPSSSLGTQ TYICNVNHP
SNTKVDKKVE PKSCDKHTC PPCPAPELLG GPSVFLFPPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN
WYVDGVEVHN AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGPREP
QVYTLPPSRE EMTKNQVSLT CLVKGFPYPSD IAVEWESNGQ PENNYKTTTP VLDSDGSFFL YSKLTVDKSR
WQQGNVFCS VMHEALHNHY TQKSLSLSPG K

FIG._4B

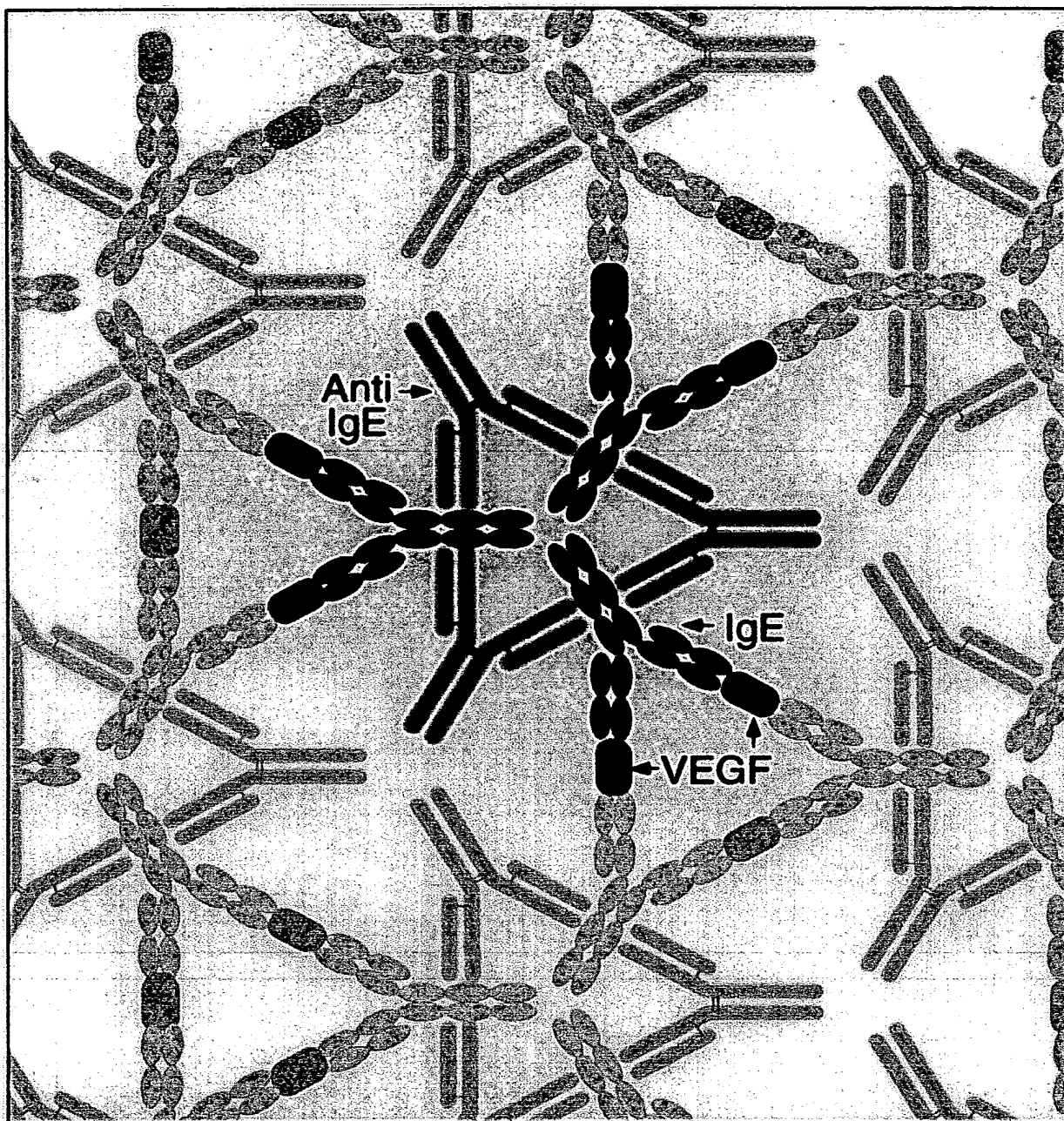


FIG. 5

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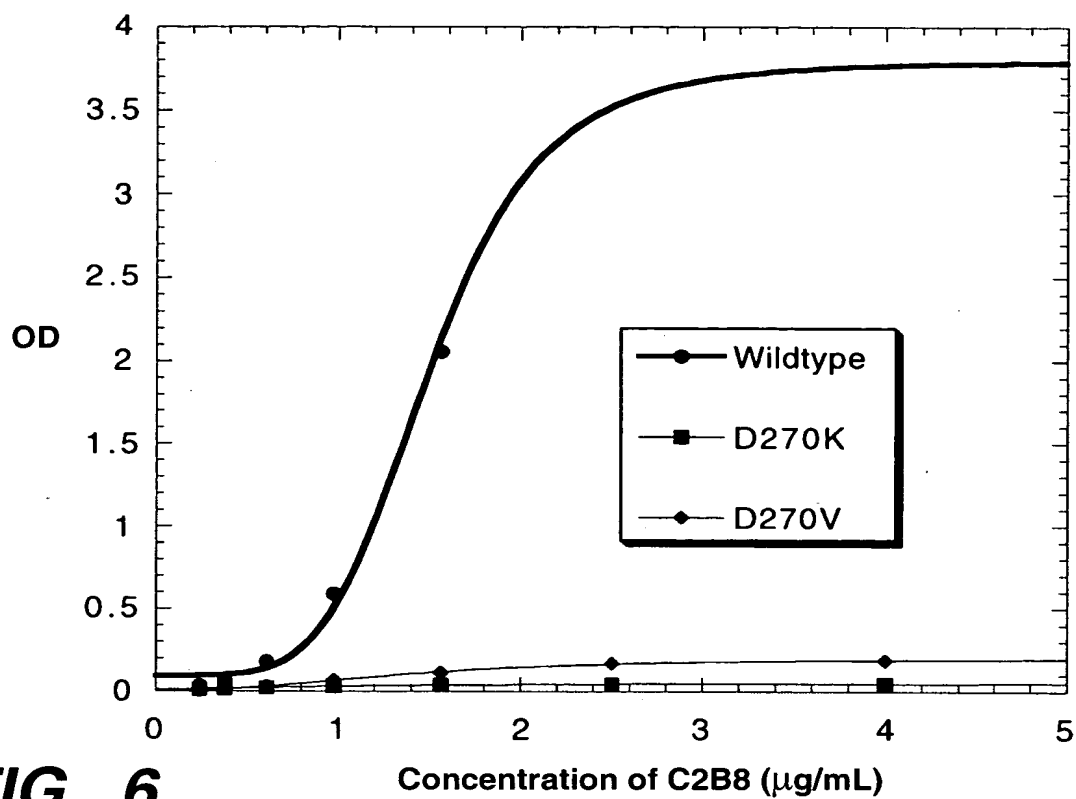


FIG. 6

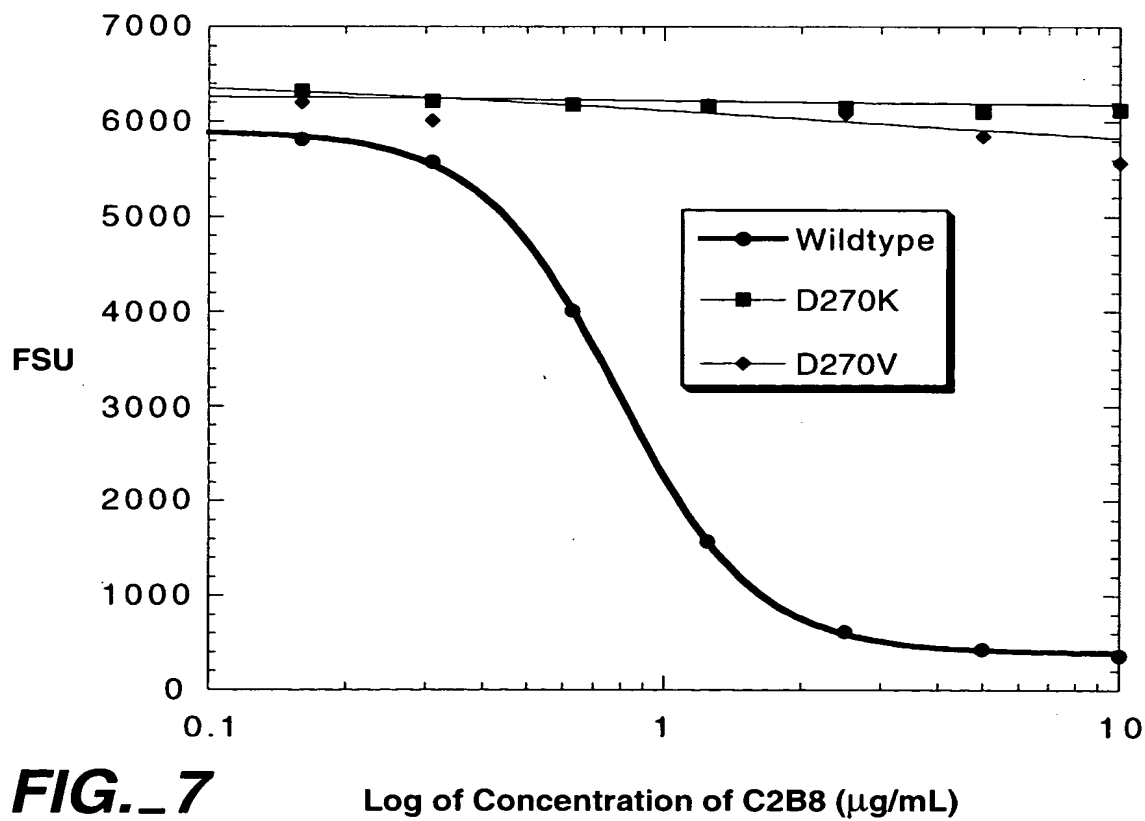


FIG. 7

Log of Concentration of C2B8 ($\mu\text{g/mL}$)

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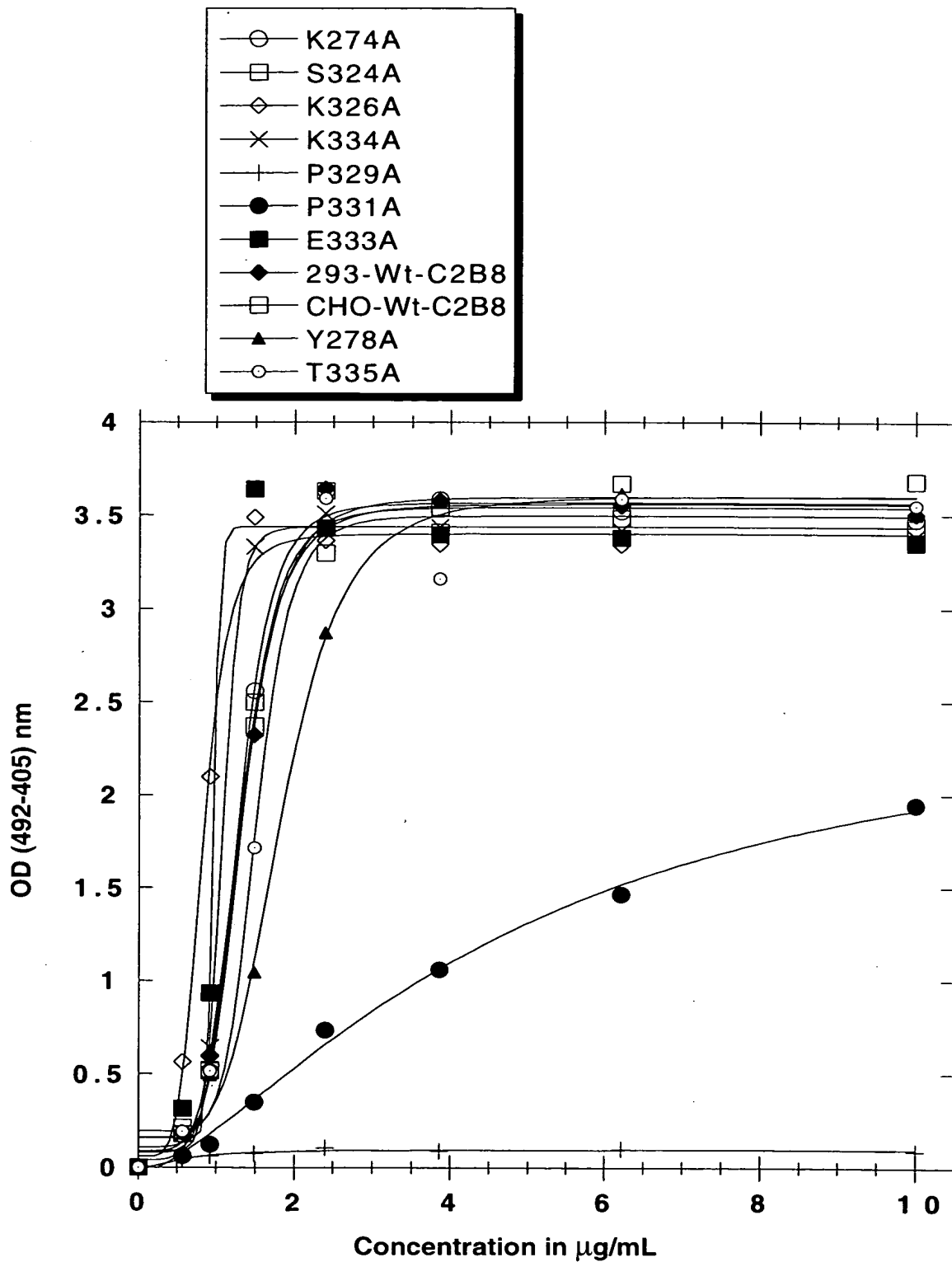


FIG._8

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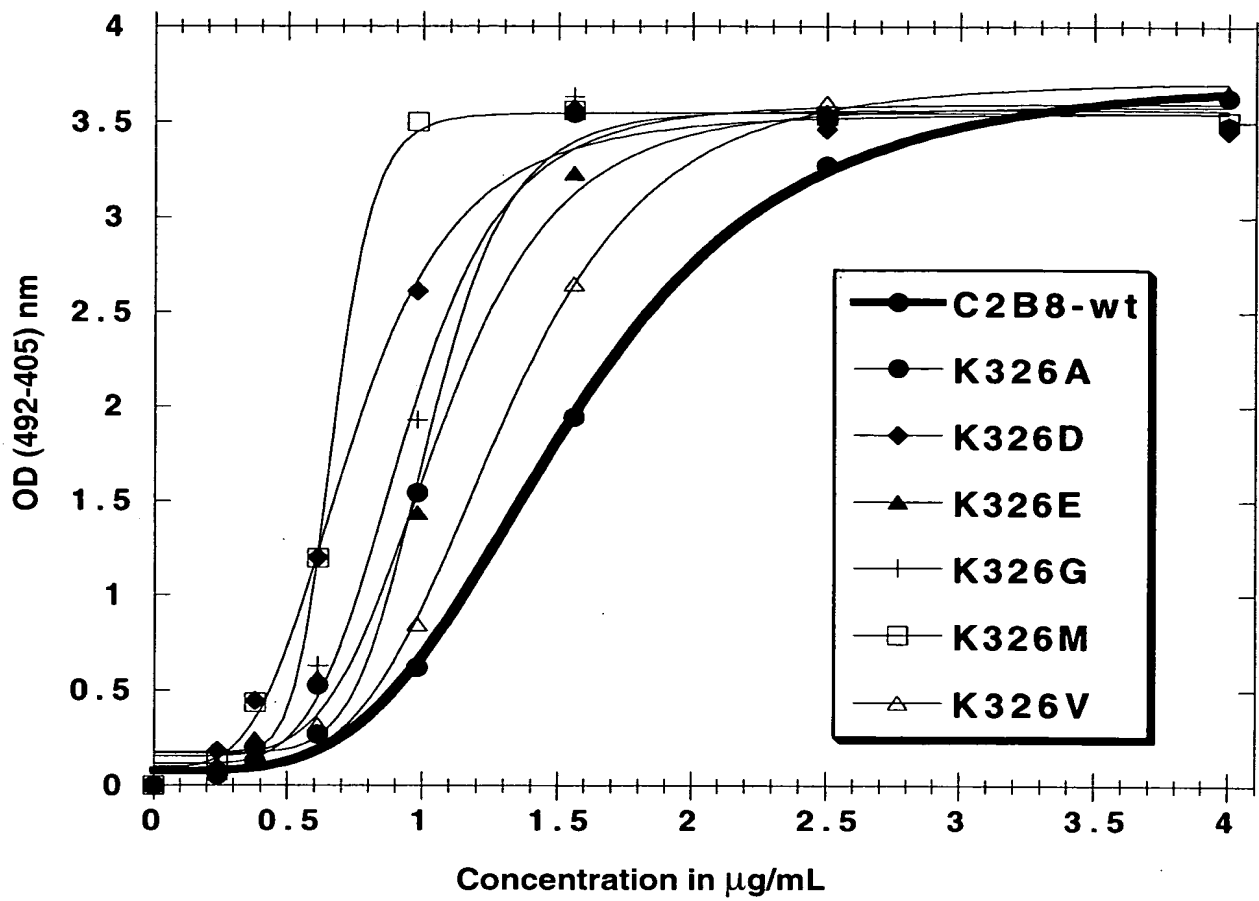


FIG._9

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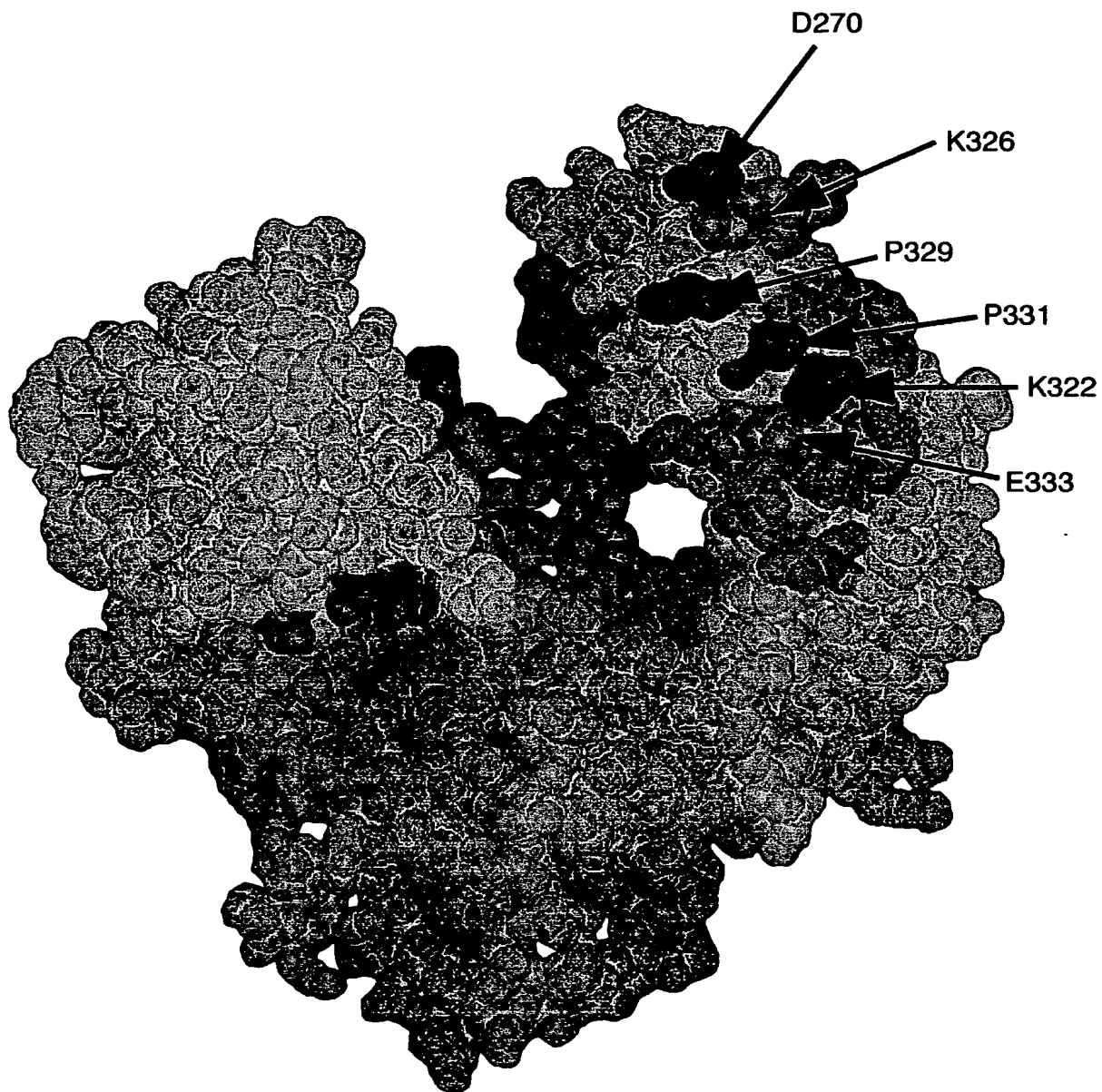


FIG._10

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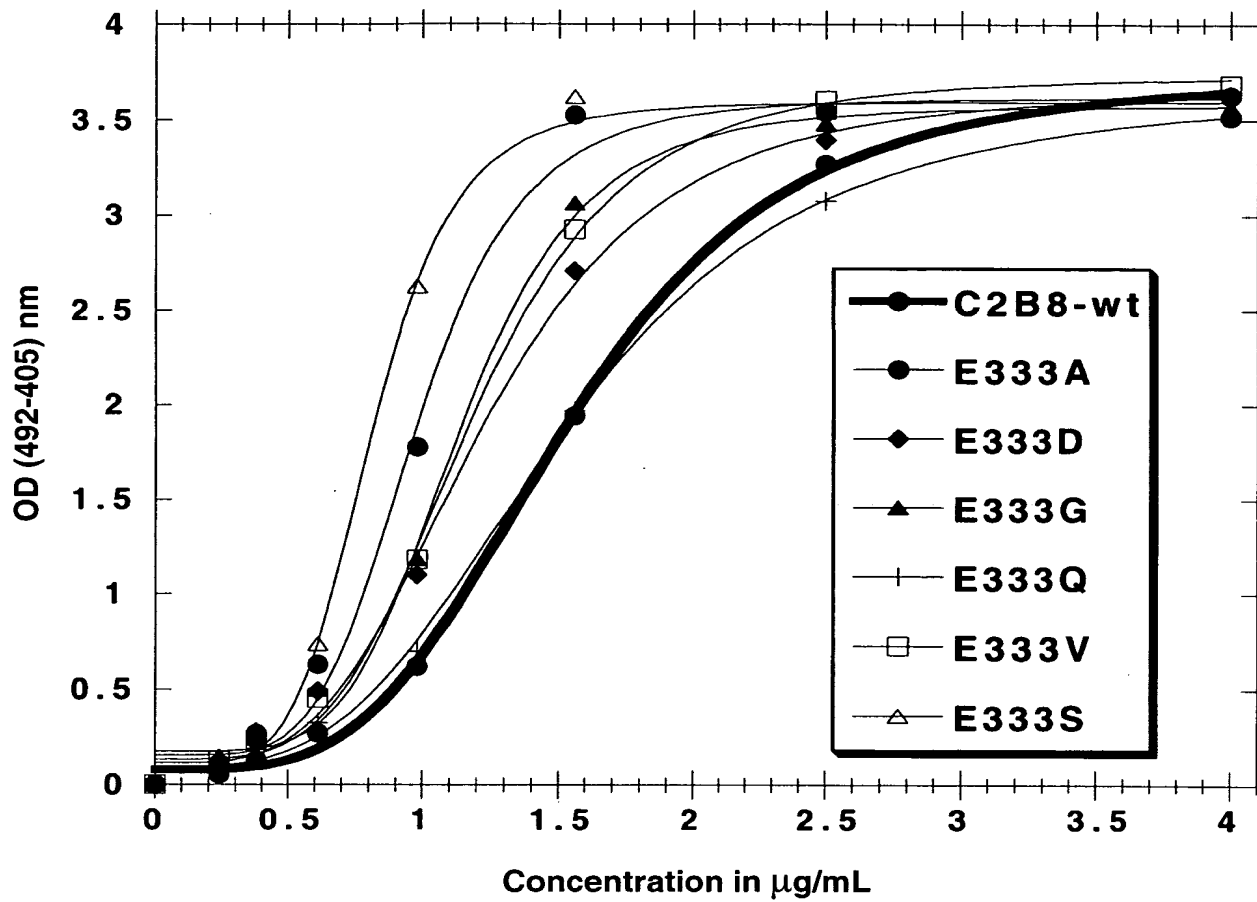


FIG._11

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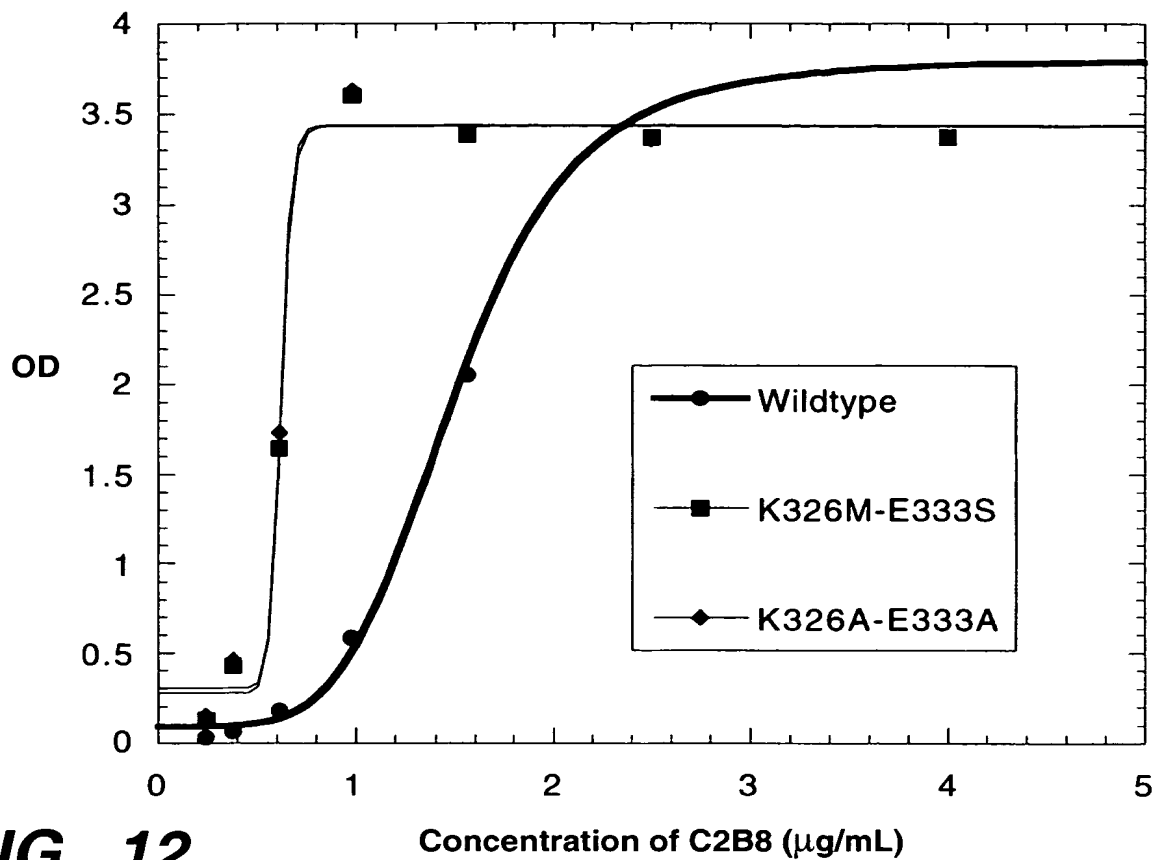


FIG. 12

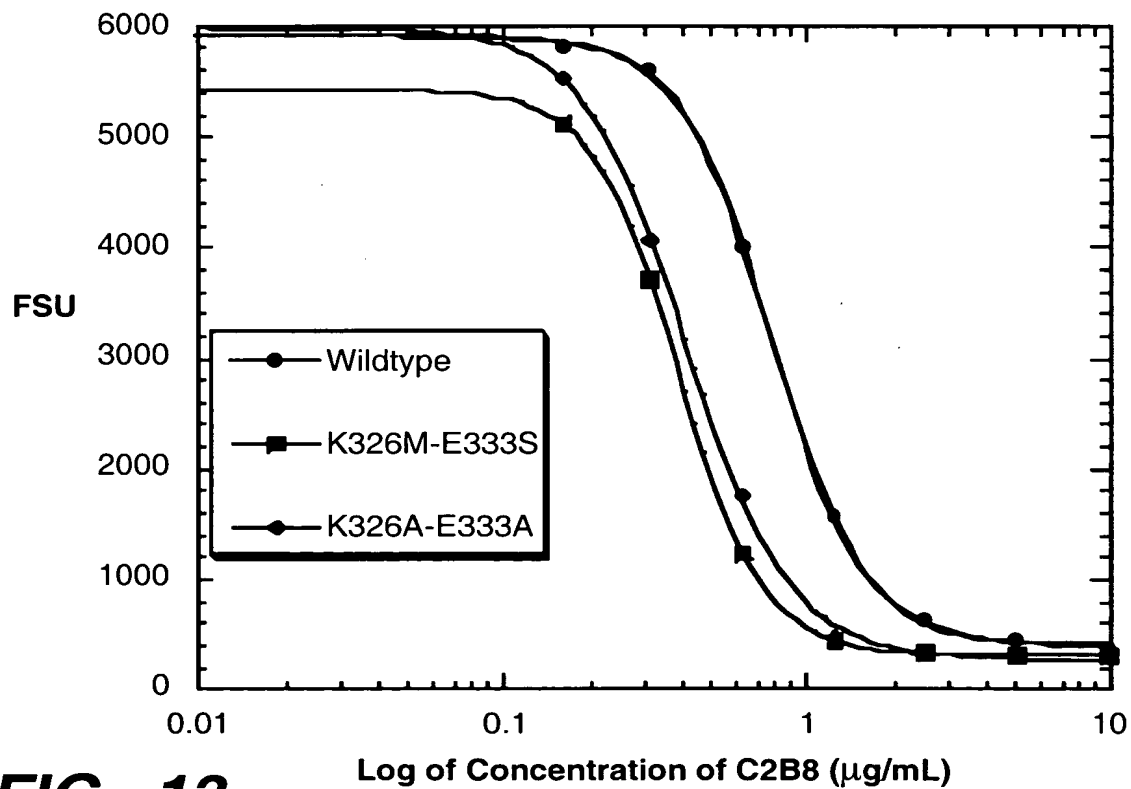


FIG. 13

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EC50 of wt-C2B8 = 1.54
EC50 of A327g (C2B8) = 1.08

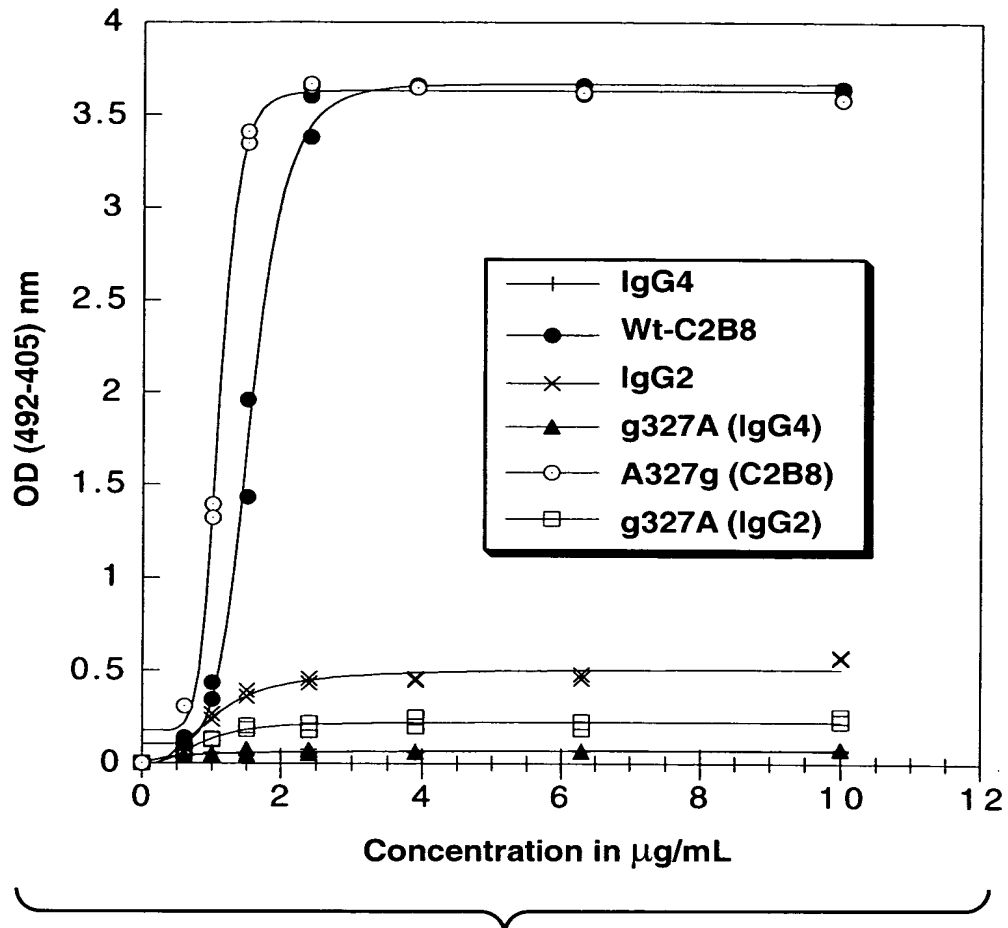


FIG._14

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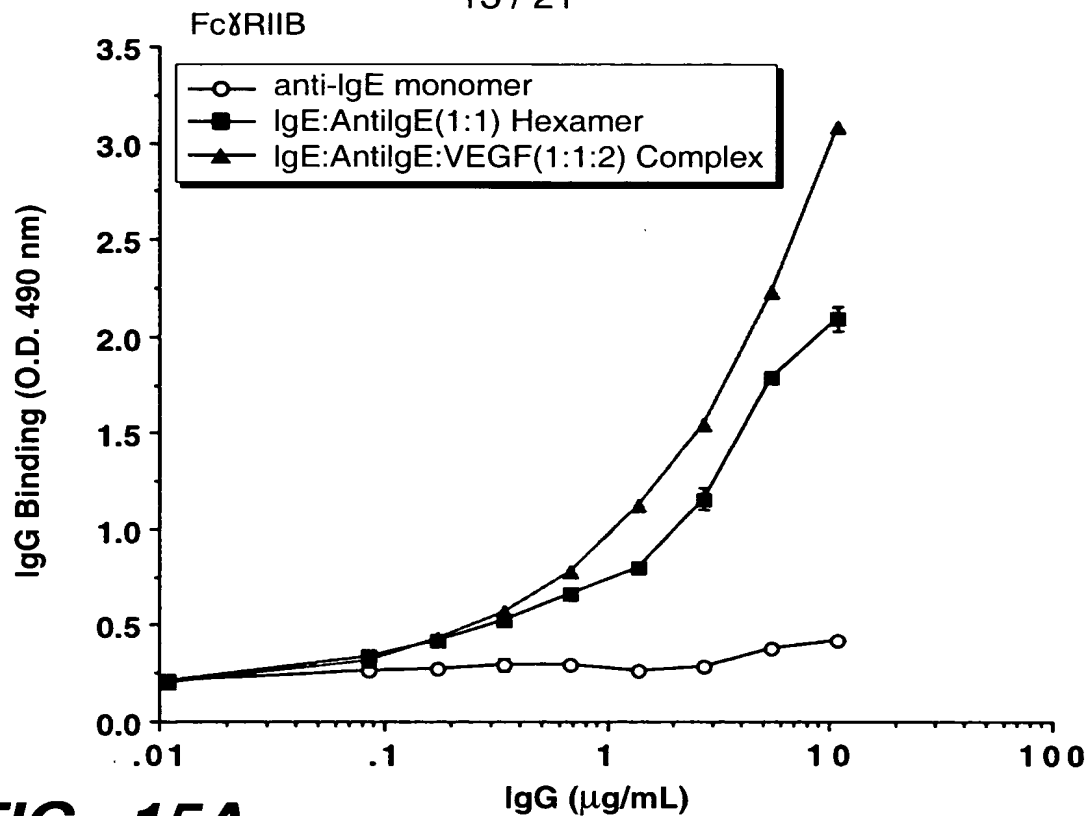


FIG. 15A

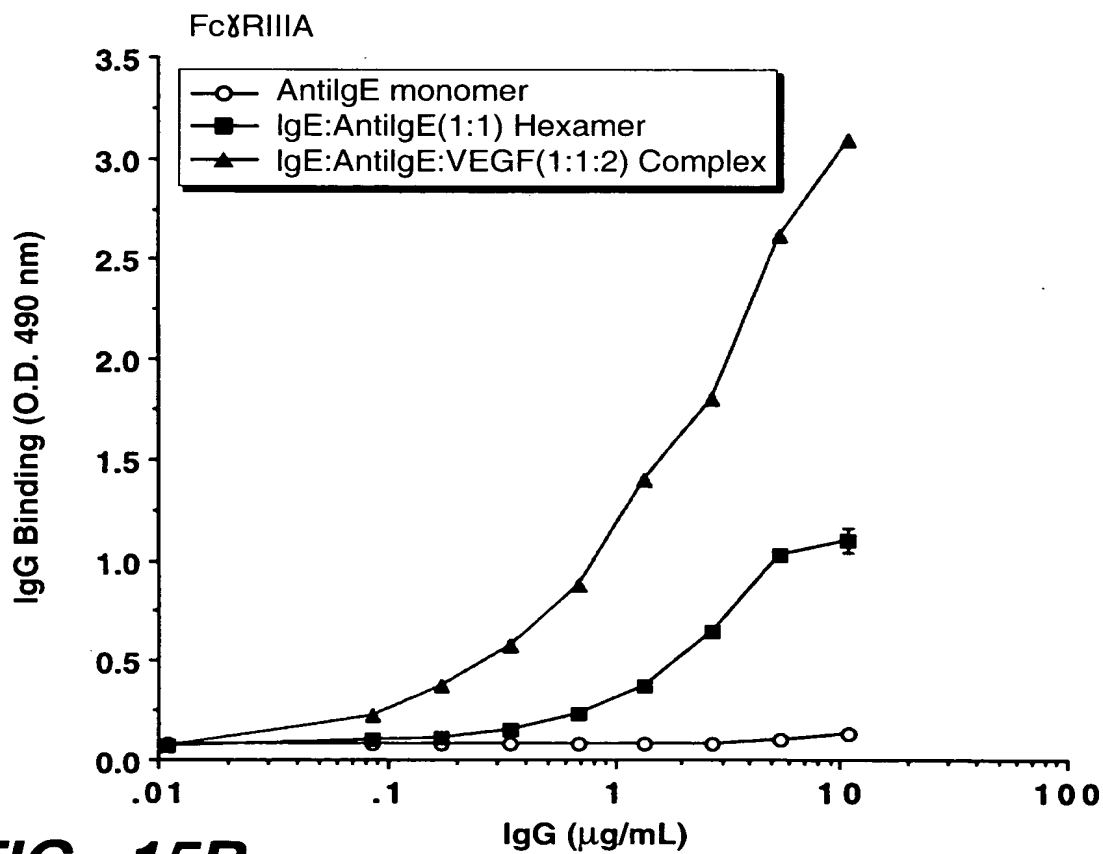


FIG. 15B

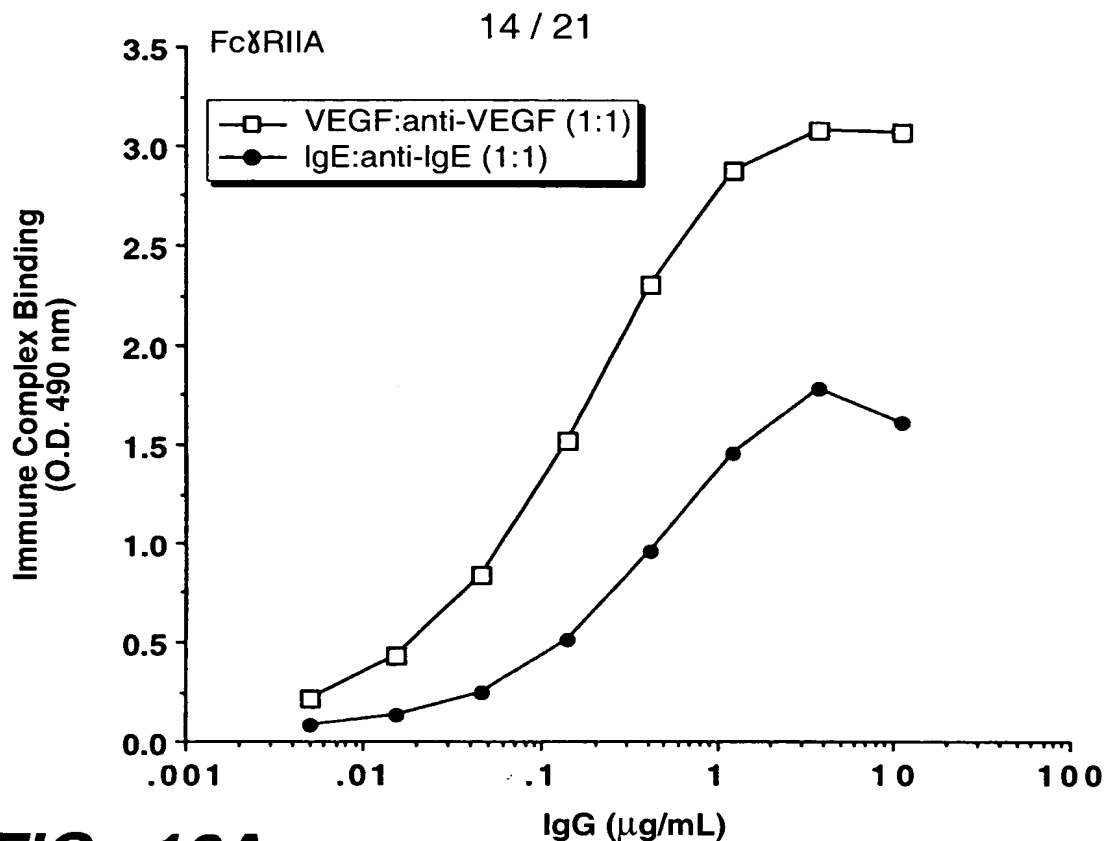


FIG._16A

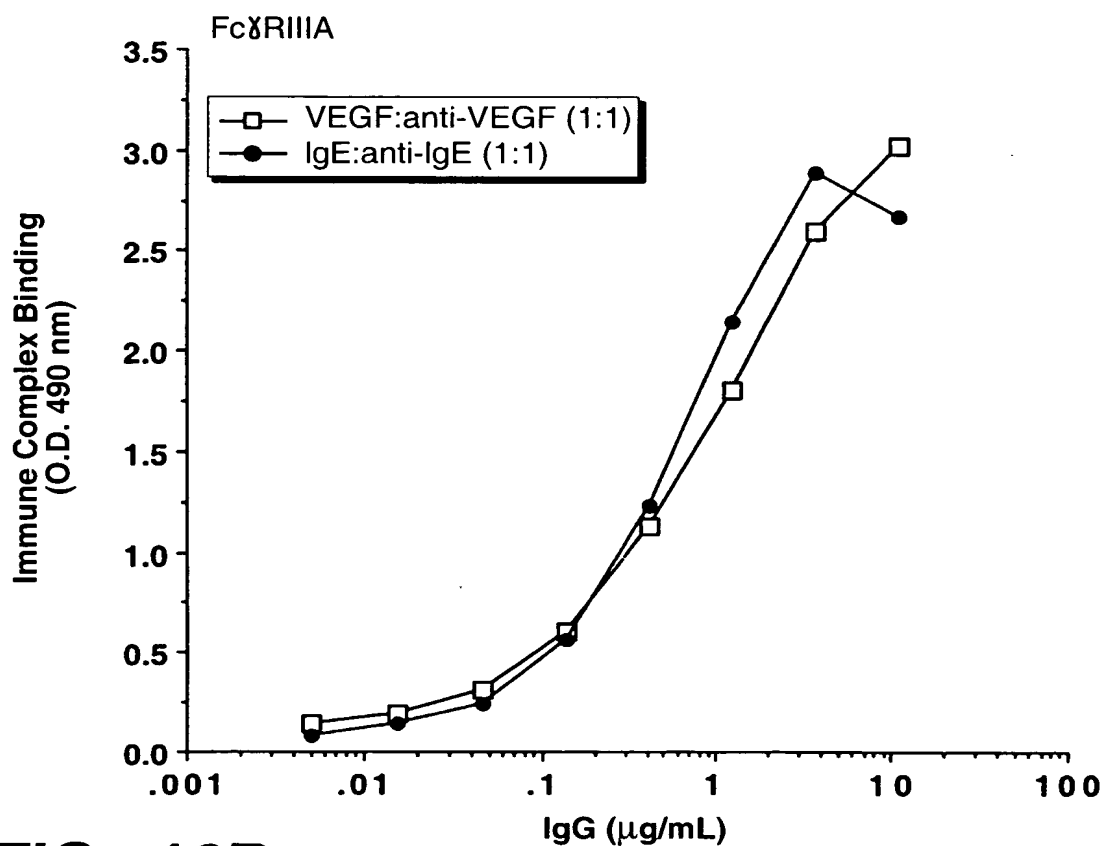


FIG._16B

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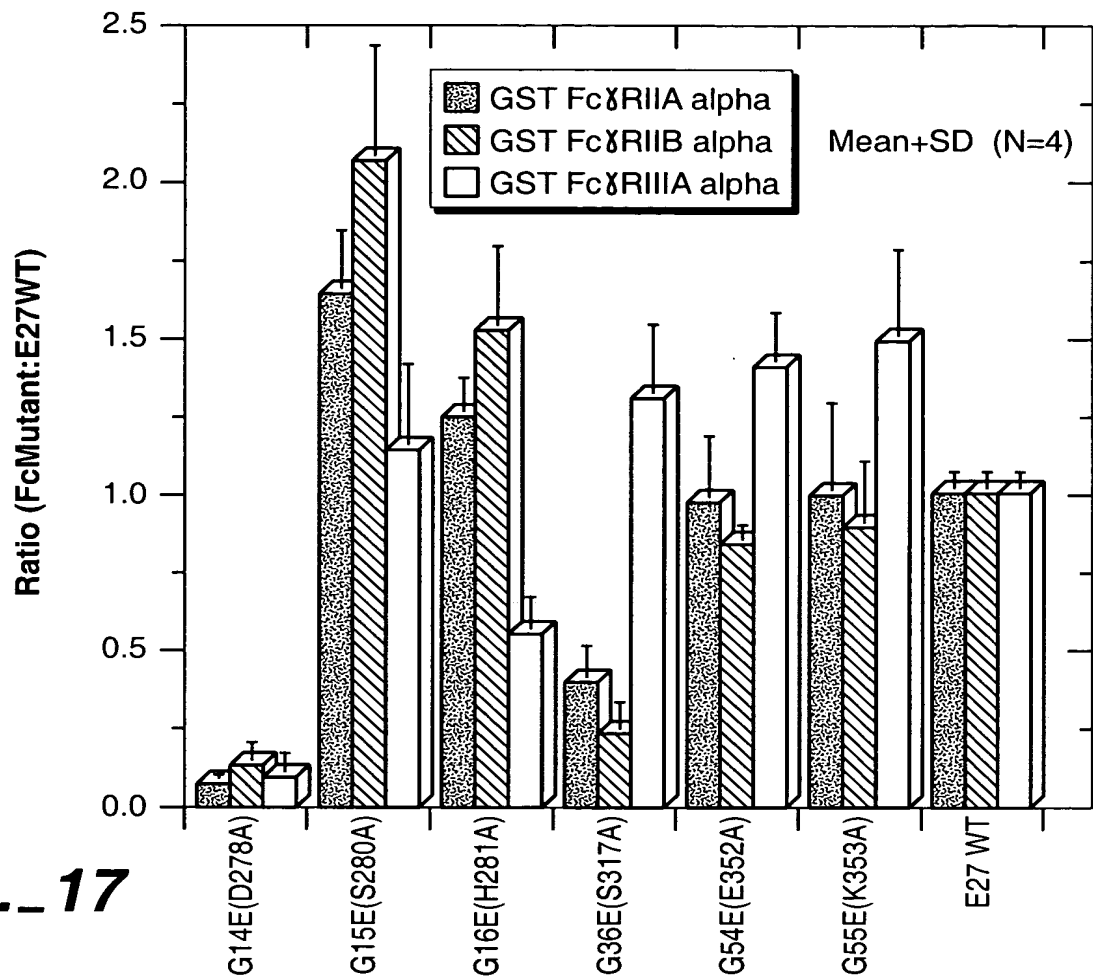


FIG. 17

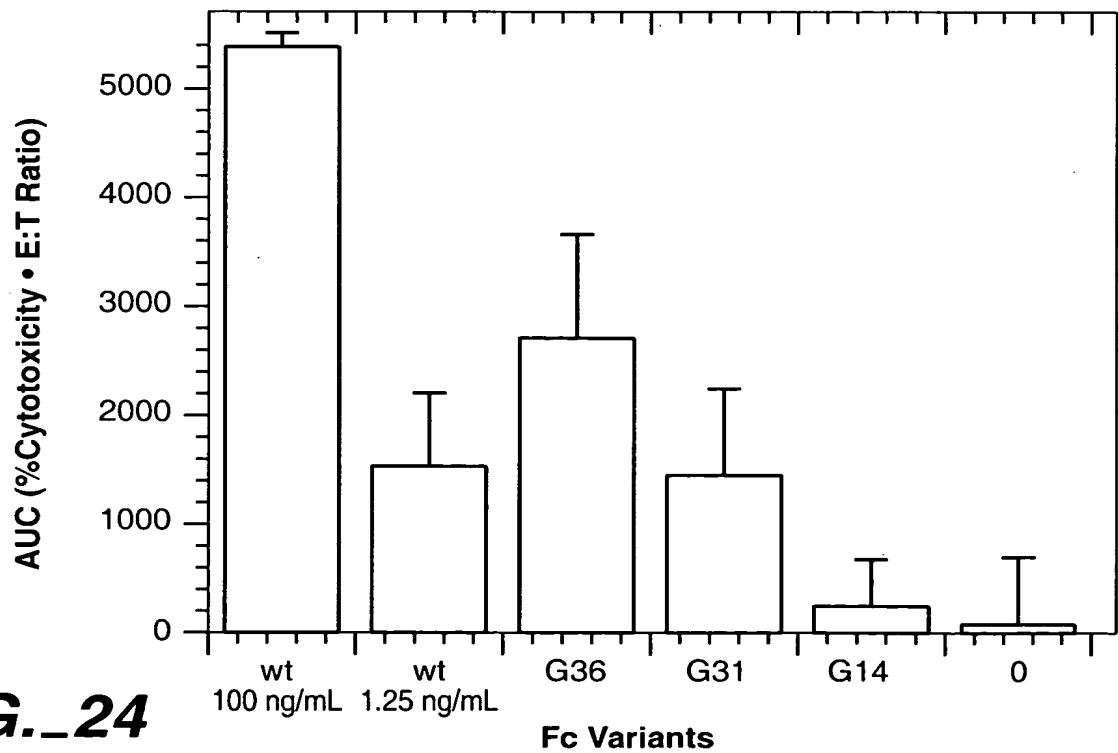


FIG. 24

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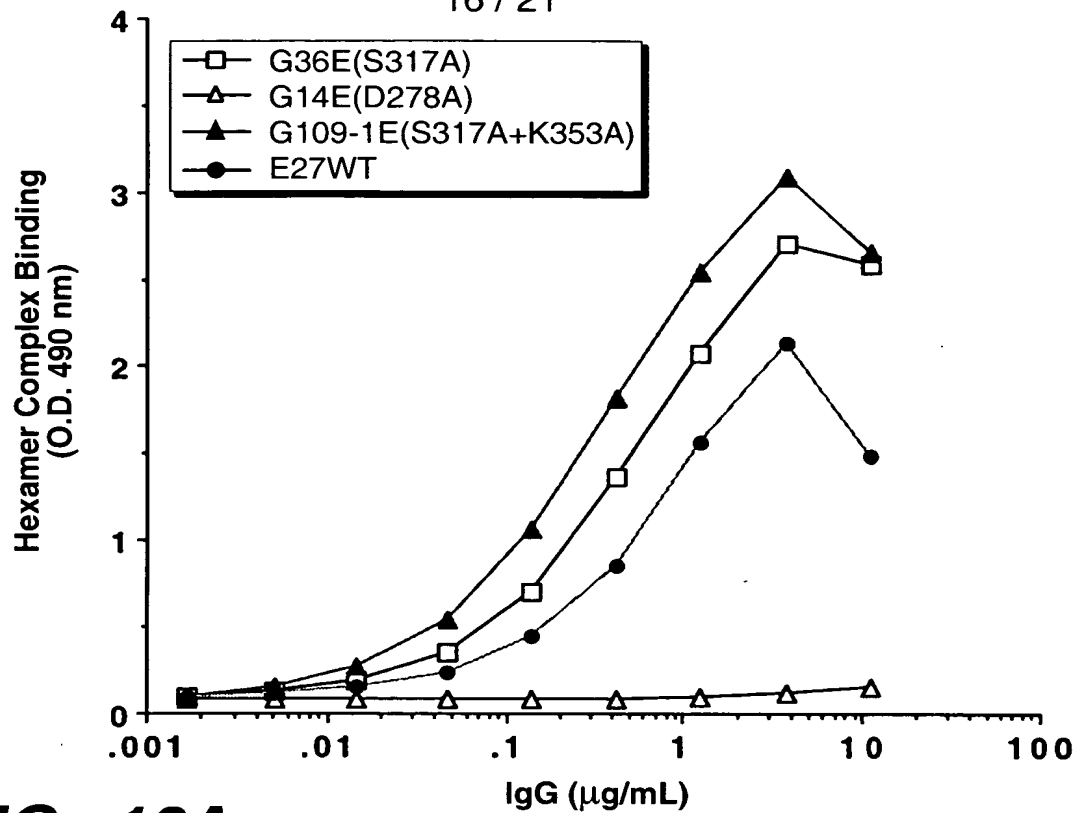


FIG._18A

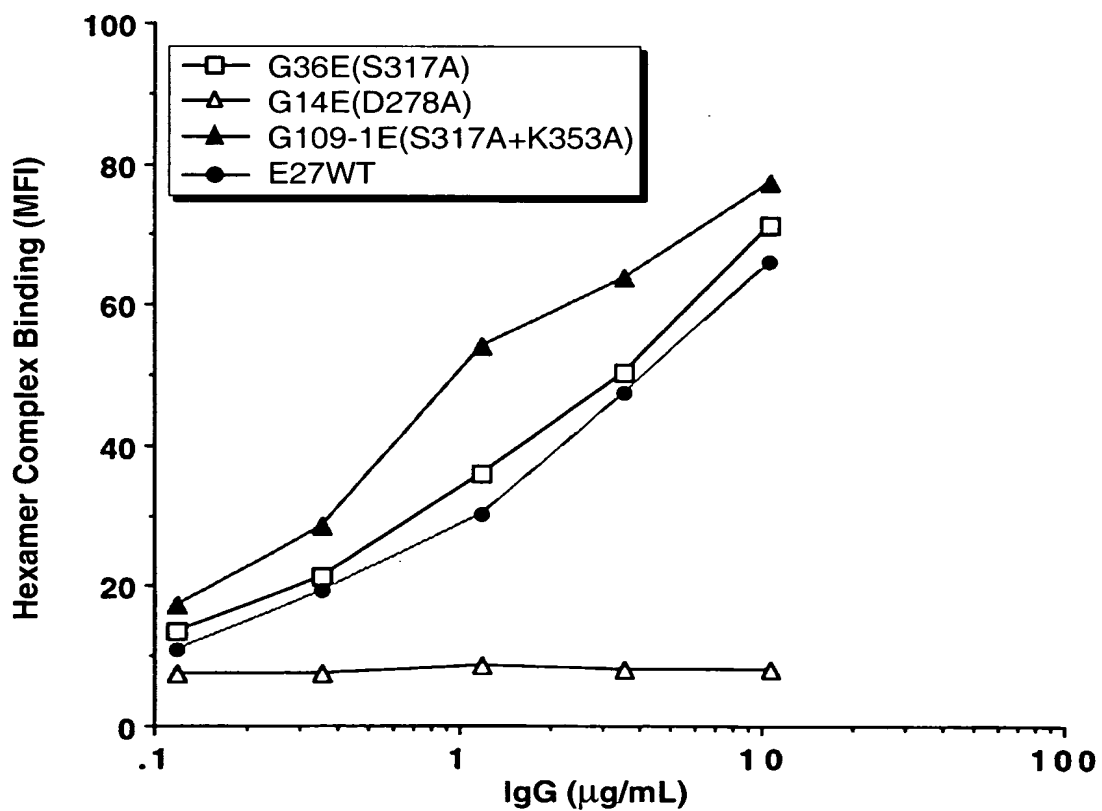


FIG._18B

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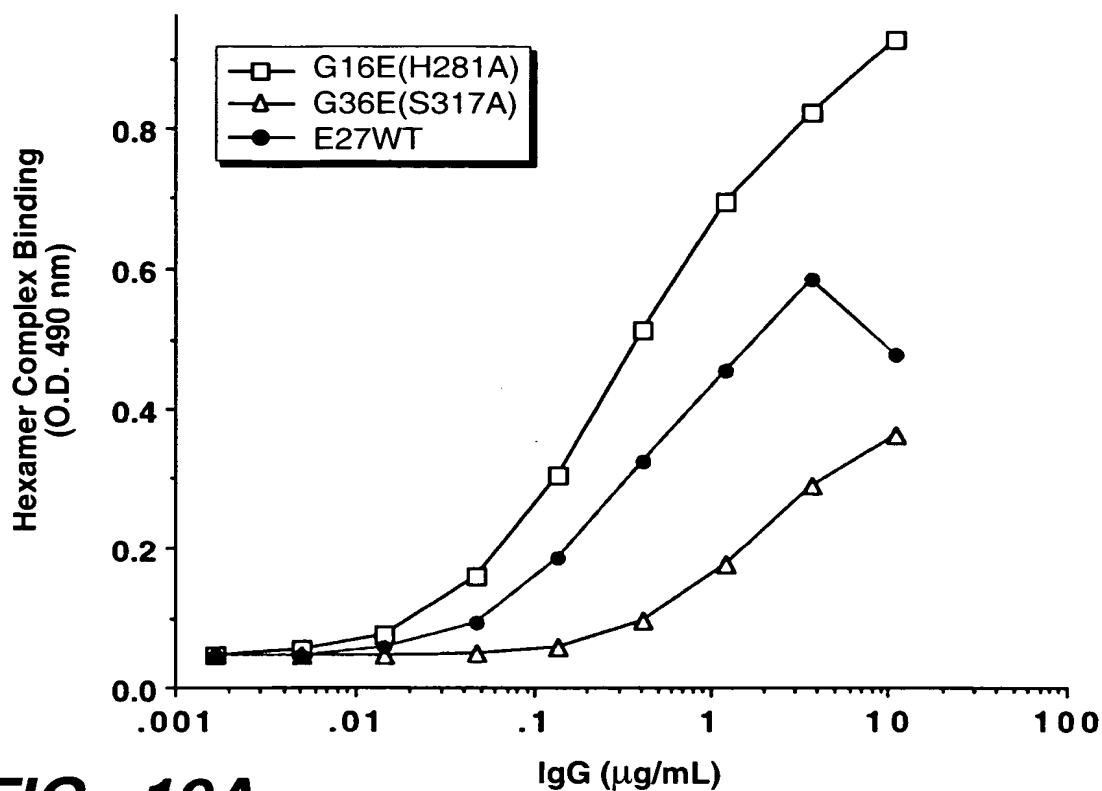


FIG. 19A

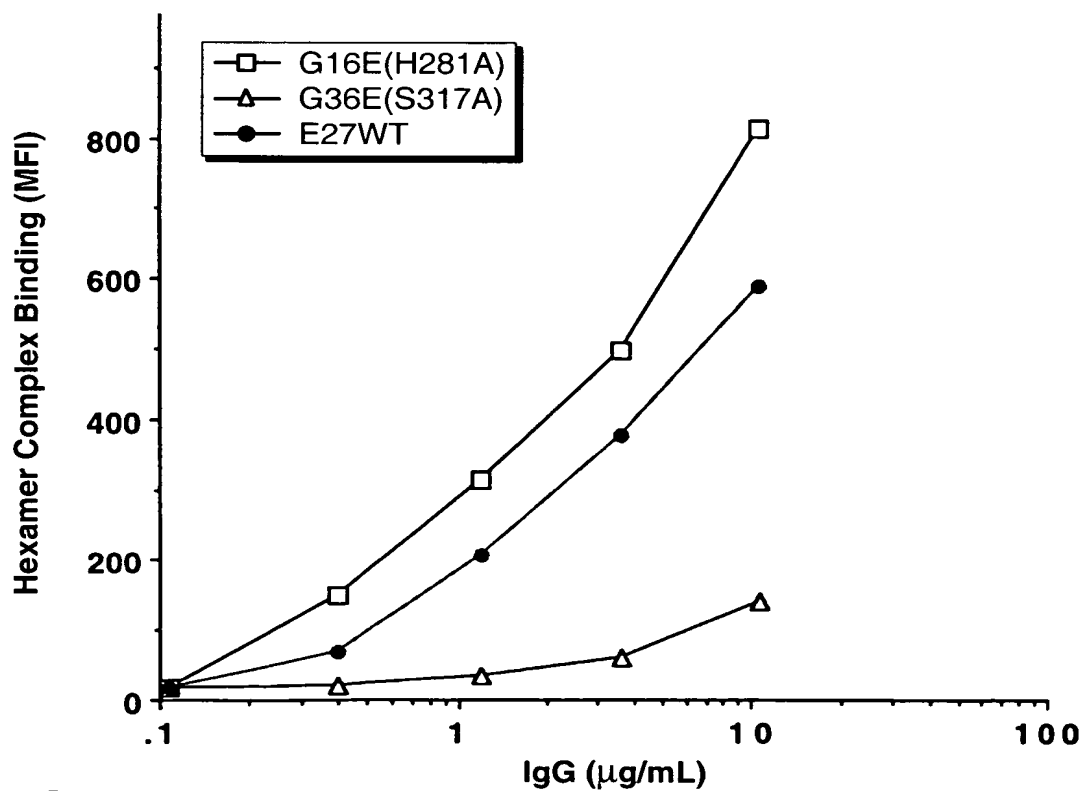


FIG. 19B

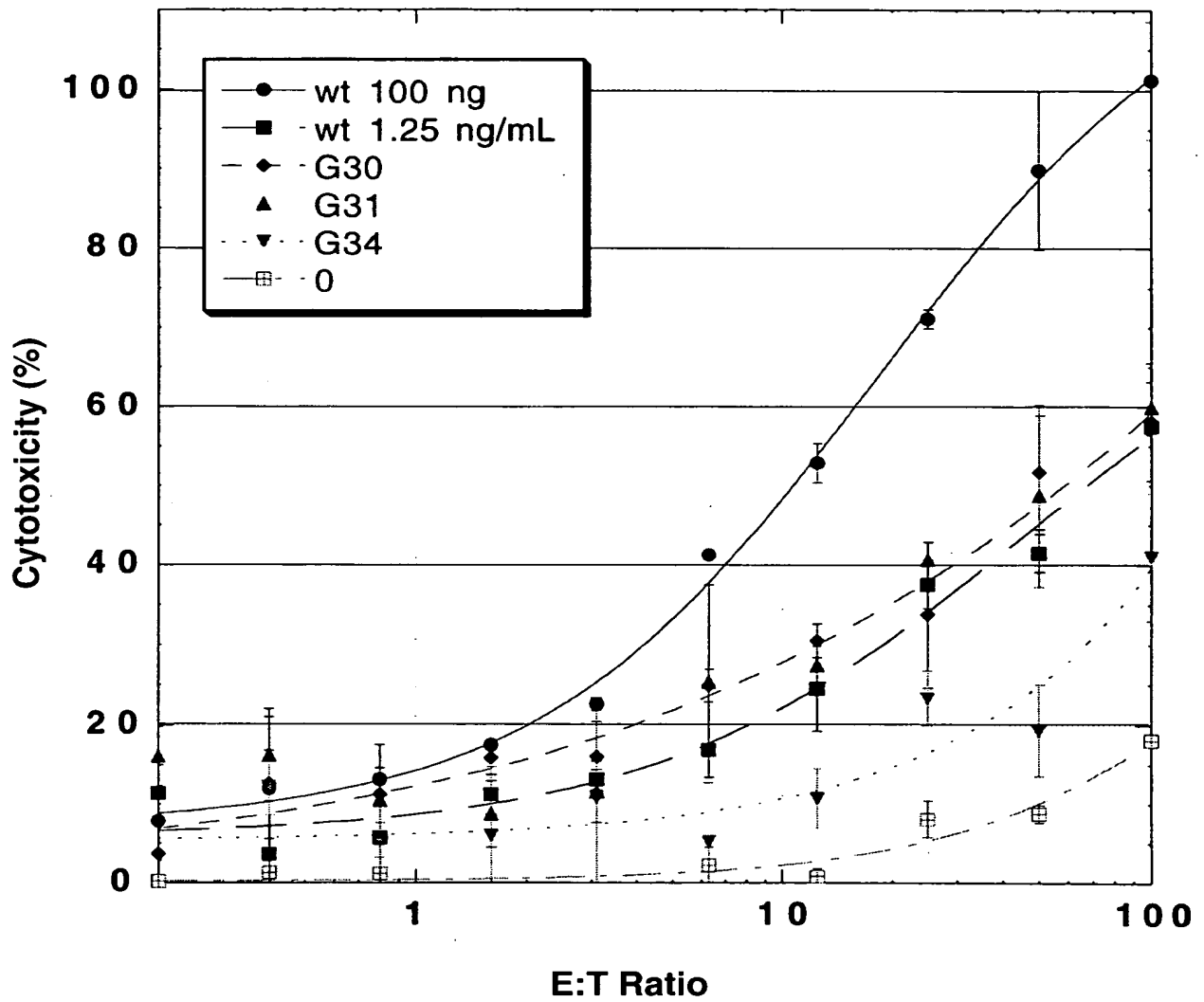


FIG._20

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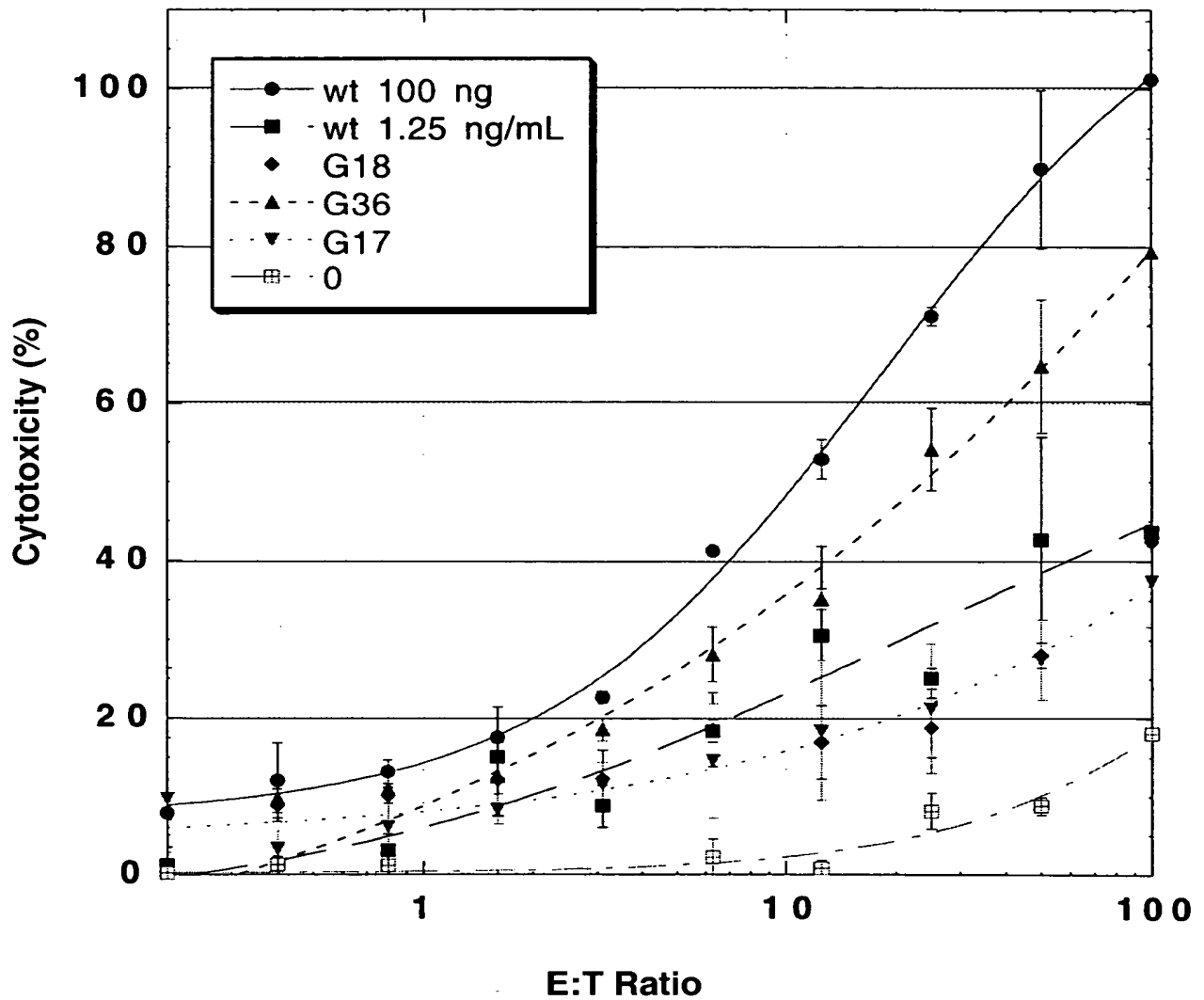


FIG. 21

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	230	240	250	260	270
humIgG1	PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV				
humIgG2	PAP - PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYV				
humIgG3	PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYV				
humIgG4	PAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYV				
murIgG1	---TVPEVSSVFIFPPKPKDVLTLTPKVTCTVVVDISKDDPEVQFSWFV				
murIgG2A	PAPNLLGGPSVFIFFPKIKDVLMLSLPIVTCVVVDVSEDDPDVQISWFV				
murIgG2B	PAPNLEGGPSVFIFFPNIKDVLMLSLTPKVTCTVVVDVSEDDPDVQISWFV				
murIgG3	PPGNILGGPSVFIFFPPKPKDALMISLTPKVTCTVVVDVSEDDPDVHVSWFV				
	280	290	300	310	320
humIgG1	DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP				
humIgG2	DGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLP				
humIgG3	DGVEVHNAKTKPREEQFNSTFRVVSVLTVLHQDWLNGKEYKCKVSNKALP				
humIgG4	DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP				
murIgG1	DDVEVHTAQTQPREEQFNSTFRSVSELPIMHQDCLNGKEFKCRVNSAAFP				
murIgG2A	NNVEVHTAQTQTHREDYNSTLRVVSALPIQHQQDWMSGKEFKCKVNNKDLP				
murIgG2B	NNVEVHTAQTQTHREDYNSTIRVVSHPPIQHQQDWMSGKEFKCKVNNKDLP				
murIgG3	DNKEVHTAWTQPREAQYNSTFRVVSALPIQHQQDWMRGKEFKCKVNNKALP				
	330	340	350	360	370
humIgG1	APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV D L				
humIgG2	APIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV				
humIgG3	APIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV				
humIgG4	SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAV				
murIgG1	APIEKTISKTKGRPKAPQVYTIPPPKEQMAKDKVSLTCLMITDFFPEDITV				
murIgG2A	APIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDFMPEDIYV				
murIgG2B	SPIERTISKPKGLVRAPQVYTLPPPAEQLSRKDVSLTCLVVGFNPGDISV				
murIgG3	APIERTISKPKGRAQTPQVYTIPPPREQMSKKKVSLTCLVTNFFSEAISV				
	380	390	400	410	420
humIgG1	EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH				
humIgG2	EWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH				
humIgG3	EWESSGQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMH				
humIgG4	EWZSNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH				
murIgG1	EWQWNGQPAENYKNTQPIMDTDGSYFVYSKLNQKSNWEAGNTFTCSVLH				
murIgG2A	EWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSQSVVH				
murIgG2B	EWTNNGHTEENYKDTAPVLDSDGSYFIYSKLNMKTSKWEKTDSEFSCNVRH				
murIgG3	EWERNGELEQDYKNTPPILSDGTYFLYSKLTVDTDVSWLQGEIFTCSVVH				
	430	440			
humIgG1	EALHNHYTQKSLSLSPGK				
humIgG2	EALHNHYTQKSLSLSPGK				
humIgG3	EALHNRFTQKSLSLSPGK				
humIgG4	EALHNHYTQKSLSLSPGK				
murIgG1	EGLHNHHTTKSLSHSPGK				
murIgG2A	EGLHNHHTTKSFSRTPGK				
murIgG2B	EGLKNYYLKKKTISRSPGK				
murIgG3	EALHNHHTQKNLSRSPGK				

FIG. 22A

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Percent Identity Among Fc Sequences

	1	2	3	4	5	6	7	8
1. humIgG1	-	94	94	94	64	66	63	68
2. humIgG2		-	93	92	65	63	60	67
3. humIgG3			-	91	64	64	61	67
4. humIgG4				-	62	64	61	64
5. murIgG1					-	65	61	67
6. murIgG2A						-	77	70
7. murIgG2B							-	68
8. murIgG3								-

FIG._22B

	230	240	250	260	270
humIgG1	PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV				
humIgG2	PAP - PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYV				
humIgG3	PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYV				
humIgG4	PAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYV				
	***				* * *
	280	290	300	310	320
humIgG1	DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP				
humIgG2	DGVEVHNAKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLP				
humIgG3	DGVEVHNAKTKPREEQFNSTFRVSVLTVLHQDWLNGKEYKCKVSNKALP				
humIgG4	DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP				
			*	*	*
	330	340	350	360	370
humIgG1	APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV				
				D L	
humIgG2	APIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV				
humIgG3	APIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV				
humIgG4	SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAV				
	**	*		*	
	380	390	400	410	420
humIgG1	EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMH				
humIgG2	EWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMH				
humIgG3	EWESSGQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMH				
humIgG4	EWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSQSVMH				
	*	*	*	*	* *
	430	440			
humIgG1	EALHNHYTQKSLSLSPGK				
humIgG2	EALHNHYTQKSLSLSPGK				
humIgG3	EALHNRFTQKSLSLSPGK				
humIgG4	EALHNHYTQKSLSLSPGK				
	**	*			

FIG._23